Focal Brain Cooling
As A New Therapy For Epilepsy

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Overview of Focal Brain Cooling

**History:**
- Bedside application in 1960’s (Ommaya *et al.* 1963, Vastola *et al.* 1969)

**Problems to Overcome:**
- Technical Issues; closed-loop system, power supply, device implantation, etc.
- Physiological Issues; optimal cooling temperatures (CBF, metabolism, neurology, etc.)

![Fig. 1: an ideal closed-loop cooling system.](image)
Focal Seizures

Video 1: simple focal seizures and SI-MI cooling. Spontaneous seizures were induced by cobalt application (20mg). Implantation site; right sensorimotor cortex. Reduction of the amplitude in epileptic discharges; around 25°C. Seizure termination; around 15°C. Figure 2: EEG before cooling (top), and during cooling (bottom).
Neurological Severity Scoring (NSS) (Shapira ver., 0-25 points (0=normal))

Normal rats

Focal seizure rats

Foot-Fault Test (%) = \frac{\text{foot-faults per limb}}{\text{steps per limb}}

Normal rats

Focal seizure rats

control (sz) 20°C(sz) 15°C(sz)

LF RF LH RH

LF RF LH RH
Laminar Changes: Receptive Field

Fig. 3: a significant decrease in the receptive fields below 15°C cooling (p<0.05; Dunnett post hoc tests).
**Fig. 4:** Cooling reduced CBF, but returned normal following rewarming. Microdialysis showed a reduction of glutamate and lactate levels during cooling.
Fig. 5: partial gliosis under the device 1 month after implantation (top; arrow). The contralateral homologous area (bottom).

Fig. 6: blood-brain barrier (BBB) permeability was elevated just after 15 °C cooling (top; Evans Blue stain), which returned to normal 1 week after 15 °C cooling (bottom).
**Video 2**: following the automatic detection of epileptic waveforms, the system started cooling down to 20°C. Cooling changed from GTC to immobility (from 6 to 1 in Racine’s scoring). **Figure 7**: the associated EEG (ipsilateral and contralateral SI-MI), cerebral temperature, and ECG.
Clinical Investigation (I)

Patient with tuberous sclerosis
(Male, 33yrs.)

Patient with parietal lobe epi.
(Female, 58yrs.)

Peltier device

↑cooling
Clinical Investigation (II)

Case 1: male, tuberous sclerosis

Case 2: female, right TLE

Case 3: male, cortical dysplasia

Glutamate (mmol/L)

Lactate (mmol/L)
Cooling down to ~15°C is able to suppress seizures with relatively normal physiological functions. The finding is a crucial step for the realization of cooling system.

Figure 8: an assumed optimal cooling curve. There is a trade-off between seizure severity and neural function, until the optimal point, $S_{opt}$. Here $f''(S_{opt})=0$. From here seizure-free is achieved only at the cost of neural function.
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References:
Thermo-Gradients

Cooling at 20°C and 5°C;
1mm: 23.3°C, 8.5°C
2mm: 24.0°C, 11.5°C
3mm: 25.4°C, 18.0°C

Cf. Inhibition of action potentials at 10°C (Volgushev et al. 2000)